中文題目：微核醣核酸與信使核醣核酸於體外人類成骨細胞老化之整合性表現
英文題目：Integrated microRNA and mRNA expression profiling in cellular senescence of human osteoblasts

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Background: MicroRNAs (miRNAs) are shown to be important regulators of biological processes and have been involved in aging processes. Age-related changes in osteoblastic functions may play a role in the pathogenesis of bone loss observed during aging. In order to study various cellular, biochemical and molecular aspects of aging of human osteoblasts, it is crucial to develop the in vitro culture system.

Method: To determine aging-specific marker miRNAs and assess their effects on cellular senescence, miRNA and mRNA profiling were performed on early and late passage cells. We employed miRSeq software package to analyze the generated Next-Generation Sequencing (NGS) data and thus obtained miRNA expression profiles. The miRNA-seq data was integrated to mRNA-seq data to observe for miRNA-mRNA functional pairs. Prediction algorithm of an online target prediction tool miRMap was used to prioritize the ranking of miRNA targets. We also incorporated the biological knowledge of Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) for identifying predominant biological themes of significant genes.

Results: The proportion of senescence-associated β-galactosidase (SA-β-gal) staining osteoblasts increased progressive especially at late passage cultures. We determined miRNA markers differentially expressed under human osteoblast culturing conditions. Twenty-nine of these miRNAs were detected in the senescent group, including 10 upregulated miRNAs and 19 downregulated miRNAs when the read counts were set to over 10 reads per million normalization (RPM). Among the differential expressed genes, a total of eighty-two genes (39 up- and 43 down-regulated genes) met the selection criteria of minimum of two-fold difference in normalized read counts between groups. Eleven target mRNAs were shown to be differentially co-expressed together with the altered nine miRNAs. The most distinctive miRNA markers, hsa-miR-1270 and has-miR-4768-5p, considered to link cellular senescence were identified. In addition, twelve significantly regulated KEGG pathways were observed.

Conclusion: Our study showed the top two pathways were MAPK and cytokine-cytokine receptor interaction pathway. Through the identification of biologically relevant miRNA markers, we can monitor the in vitro aging process. Both miR-1270 and miR-4768-5p may apply to future elucidation of the potential molecular mechanism related to the cellular senescence of human osteoblasts.

Keywords: *miRNAs, cellular senescence, aging, human osteoblast.*